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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
SHAFER, SHULAMITH H	
ART UNIT	PAPER NUMBER
1647	
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12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,691	DAVIDS ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/15/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,4-15 and 17-78* is/are pending in the application.

4a) Of the above claim(s) *4-9,17-19 and 22-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10-15,20,21 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

The amendment received 15 September 2008 has been entered. Claims 1, 4-15 and 17-78 are pending in the instant application. Claim 1 has been amended and the amendment made of record. Claims 4-9, 17-19, and 22-77 are withdrawn as being directed to a non-elected invention. Claims 1, 10-15, 20, 21 and 78 are under consideration.

Applicants have submitted Exhibit 1which details experiments carried out using the INSP052EC protein and two post-filing date references Chung et al. and Moh et al. These documents will be discussed below.

Priority:

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on 30 April 2002. A certified copy of UK 0209884.6 was submitted on 16 June 2008. Therefore, benefit of priority is granted to 30 April 2002.

Withdrawn Rejections

The rejection of Claims 1, 10-15, 20 and 21 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants amendment to the claims.

Maintained/New Rejections and/or Objections

Double Patenting Rejection:

The rejection of Claims 1, 15 and 78 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30, 31, and 39 of

co-pending application 10/579,113 is maintained for reasons of record and for reasons set forth below.

Applicants traverse the rejection (Response of 15 September 2008, page 13, Section III). The reasons for the traversal are:

Applicants assert that co-pending application 10/579,113 has not yet been examined. Therefore, the rejection should be withdrawn or should be a provisional one.

Applicants' attention is directed to MPEP § 804 which states:

> Occasionally, the examiner becomes aware of two copending applications that were filed by the same inventive entity, or by different inventive entities having a common inventor, and/or by a common assignee, or that claim an invention resulting from activities undertaken within the scope of a joint research agreement as defined in 35 U.S.C. 103(c)(2) and (3), that would raise an issue of double patenting if one of the applications became a patent. Where this issue can be addressed without violating the confidential status of applications (35 U.S.C. 122), the courts have sanctioned the practice of making applicant aware of the potential double patenting problem if one of the applications became a patent by permitting the examiner to make a "provisional" rejection on the ground of double patenting. *In re Mott,* 539 F.2d 1291, 190 USPQ 536 (CCPA 1976); *In re Wetterau,* 356 F.2d 556, 148 USPQ 499 (CCPA 1966). The merits of such a provisional rejection can be addressed by both the applicant and the examiner without waiting for the first patent to issue.
>
> **The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application** unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications.

It is noted that this rejection was made as a provisional double patenting rejection in the previous Office Action.

35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 12-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims, as recited, read on compounds that exist in nature, and encompass naturally occurring macromolecules such as proteins, DNA and antibodies. Claim 14 recites that the compound is a natural

substrate.. There is no limitation wherein the recited compound is isolated or otherwise modified. Thus, the claims, as written, do not sufficiently distinguish over a naturally occurring compound because the claims do not particularly point out any non-naturally occurring differences between the claimed compounds and naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. (See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of language indicating an "isolated" compound (See MPEP 2105).

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10-15, 20, 21 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, the independent claim of the instant invention is drawn to a polypeptide which (i) comprises or consists of amino acids of SEQ ID NO:16 or 26 or (ii) consists of the amino acids of SEQ ID NO:20 or (iii) is a fusion protein comprising a polypeptide according to i) or ii) or comprising a fragment of a polypeptide according to i) or ii) fused to a heterologous polypeptide. The specification identifies:

SEQ ID NO:16 as the INSP052 polypeptide (amino acids 1-416),

SEQ ID NO:26 as the mature INSP052 polypeptide, that is the polypeptide of SEQ ID NO:16 minus the first 33 amino acids (signal sequence) (identical to amino acids 34-416 of SEQ ID NO:16);

SEQ ID NO:20 is the extracellular domain of INSP052 (identical to amino acids 1-240 of SEQ ID NO:16)

SEQ ID NO:22 is the extracellular domain of the mature INSP052 polypeptide, (identical to amino acids 34-240 of SEQ ID NO:20, amino acids 34-240 of SEQ ID

NO:16 and amino acids 1-207 of SEQ ID NO:26) [paragraph 0029 of PGPUB 20040204352, the PGPUB of the instant invention].

The claim, as written, is confusing in reciting a polypeptide which **comprises or consists** of the recited sequences. These terms have vastly different meanings. The use of "comprising or consisting of" language is especially confusing because claim 1(iii) requires the fusion polypeptide to comprise a polypeptide of i) or ii). If the claimed polypeptide consists of SEQ ID NO:16 or 26, then said polypeptide cannot have anything added to it. It is suggested that applicants amend the claims to recite a polypeptide "comprising the amino acid sequences…..", " a polypeptide consisting of the amino acid sequences…" and claims to a fusion polypeptide as separate claims.

Claim 1 has been amended to read "wherein the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO:22". As noted above, a sequence which consists of "amino acid sequence as recited in SEQ ID NO:16 or SEQ ID NO:26…" cannot have any other components. Furthermore, as noted above, the amino acid sequences of SEQ ID NOs:16, 26, and 20 all comprise the extracellular domain of the INSP052 polypeptide. It is unclear if applicants intend the claimed polypeptide to comprise only one extracellular domain (which is present in the amino acid sequences of SEQ ID NOs:16, 26, and 20) or to comprise the extracellular domain present in the amino acid sequences of SEQ ID NOs:16, 26, and 20 and the additional extracellular domain of SEQ ID NO:22, *i.e.* at least two amino acid sequences each of which comprises the extracellular domain.

The rejection of Claims 13 and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record and for reasons set forth below.

Claim 13 is vague and indefinite in reciting "A compound that either increases or decreases the level of expression or activity of a polypeptide.....without inducing any of the biological effects of the polypeptide" It is unclear how one can increase the biological activity of a polypeptide without inducing biological effects of said peptide. Furthermore, the specification does not identify any specific biological activity or effect

nor does it distinguish or define the "biological activity of the polypeptide" and "the biological effects of the polypeptide". Without specific definitions it would be unclear to one skilled in the art what is encompassed in this phrase.

Claim 14 is included in this rejection as dependent upon claim 13.

Applicants traverse the rejection (Response of 15 September 2008, page 14, paragraph 5). The reasons for the traversal are:

As described in the specification as filed at page 41, lines 23-28, the claim describes the situation wherein "binding of the polypeptide to normal cellular binding molecules may be inhibited, such that the normal biological activity of the polypeptide is prevented". Thus, when read in view of the specification, the claim is definite.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

The section in the specification identified by Applicants (page 41, lines 23-28) is directed to expression vectors encoding fusion proteins comprising the polypeptide of the invention fused to histidine residues. There are no teachings of a compound which either increases or decreases the level of expression or activity of a polypeptide. Furthermore, the traversal has not addressed the rejection of how a compound may increase the biological activity of a polypeptide without inducing biological effects of said peptide.

Claim 78, which depends from claim 1 (iii), is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is unclear, as written, in that it depends from only part of Claim 1 ("according to claim 1(iii)…"). Additionally, the claim is vague and indefinite in reciting "a fusion protein comprising a fragment which **comprises or consists** of the amino acid sequence as recited in SEQ ID NO:20 or in SEQ ID NO:22 fused to a heterologous polypeptide.". These terms have vastly different meanings and thus the metes and bounds of the claim cannot be determined. (See discussion above). Furthermore, it is unclear if applicants intend the

fusion protein to comprise one extracellular domain comprising of SEQ ID NOs:20 or 22, or multiple extracellular domains comprising additional sequences of SEQ ID NOs:20 or 22 (additional fragments) as recited in Claim 78.

Additional claims are included in this rejection as dependent upon rejected claims.

35 U.S.C. § 112, First Paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 1, 10-15, 20, 21 and 78 under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a fusion polypeptide which comprises the amino acid sequence as recited in SEQ ID NOs:16, 20, or 26 fused to a heterologous polypeptide that has an activity that is an antagonist of TNF-alpha, IL-4, IL-6 and or IL-2 does not reasonably provide enablement commensurate with the full scope of the claim is maintained for reasons of record and for reasons set forth below.

Claim 1, the independent claim of the instant invention has been amended and is now drawn to an isolated polypeptide which is a fusion protein comprising a polypeptide according to (i) or (ii) or comprising a fragment of a polypeptide according to (i) or (ii) fused to a heterologous polypeptide; wherein the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO:22;

The claim can reasonably be interpreted as being drawn to a fusion protein comprising a fragment of any one of SEQ ID NOs: 16, 20, or 26 fused to a heterologous polypeptide which functions as an antagonist to expression and/or secretion of any cytokine.

The specification does not provide adequate guidance as to how to *make* functional species comprising fragments of SEQ ID NOs: 16, 20, or 26, nor how to *use* those that are not, which would be expected to be the majority of species.

There is no guidance presented in the specification as to how to make and/or use fusion proteins comprising fragments of any one of SEQ ID NOs:16, 20, or 26 fused to heterologous polypeptides. Insufficient teaching is presented as to which fragments of the full length proteins must be retained in order to arrive at a functional protein. While one of skill in the art may construct a fusion protein comprising any given fragment of a protein, it would require undue experimentation to determine which fragments would maintain the functioning envisioned in the claims of the instant invention. The specification provides no teachings as to which domains of the molecules must be conserved in the fusion proteins in order to retain the function of a cytokine antagonist. Claim 1 has been amended to recite "wherein the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO:22". However, even if an active or binding site, such as the extracellular domain (SEQ ID NO:22), were identified in the specification, this would not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore the presence of unspecified fragments of SEQ ID NOs:16 or 26, which comprise the full length protein, including the signal sequence or the mature protein or SEQ ID NO:20, which comprises the extracellular domain plus the signal sequence may not be sufficient to retain the required activity of functioning as an antagonist of cytokine expression and/or secretion.

Claim 1 has been amended to recite "wherein the polypeptide functions as an antagonist of cytokine expression and/or secretion." Thus, the claim is broadly drawn to a polypeptide which antagonizes any, unspecified cytokine expression and /or secretion. The specification teaches that the extracellular domain of INSP052 (also referred to herein as INSP052EC) downregulates TNF-alpha, IL-4 and IL-2 secretion *in vitro* in a Concanavalin A (ConA) stimulated human peripheral blood mononuclear cells

(hPBMC) assay. Delivery of INSP052EC cDNA in an *in vivo* model of fulminant hepatitis (animals treated with ConA) decreases TNF-alpha and m-IL-6 levels in serum of treated animals [paragraph 0026, 0027]. Thus, the specification teaches that the polypeptides of the instant invention are inhibitory of the pro-inflammatory cytokines TNF-alpha, IL-4, IL-2 and IL-6. There are no teachings as to the effect of the polypeptides of the instant invention of expression or secretion of any of the myriad of other cytokines.

Thus, one of skill in the art would be unable to predict that a fusion polypeptide comprising **unspecified fragments** of SEQ ID NOs:16, 20 or 26 would be able to function as an antagonist of the expression or secretion of **any**, **unspecified cytokine**.

Applicants traverse the rejection (Response of 15 September 2008, Section V, pages 16-17, 4th paragraph). The reasons for the traversal are:

1. The pending claims have been amended herein such that claim 1 specifically requires that the isolated polypeptide comprises or consists of i), ii), or iii), and that the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO: 22.

2. Applicants have presented Exhibit 1. Exhibit 1 details experiments utilizing the extracellular domain of INSP052, the 1NSP052EC protein (SEQ ID NO: 22). All fragments containing the extracellular domain would share the required biological activity of the active fragment upon which the experiments are based. Applicants argue that the experimental evidence provided in Exhibit 1 shows that 1NSP052 is useful in treating various autoimmune/inflammatory disorders.

3. Applicants assert INSP052 is also identical to a protein described in the literature as Hepatocyte cell adhesion molecule (hepaCAM) and have submitted post-published references such as Chung et al. and Moh et al. to provide evidence of the role of INSP052 in wound healing.

4. The specification teaches the skilled person to identify fragments that contain an immunoglobulin domain (page 8 of the application as filed) and the functional importance of this domain (page 16, line 4-9 of the application as filed).

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

In response to 1: While Claim 1 has been amended to recite a polypeptide comprising an extracellular domain of SEQ ID NO:22, 1(iii) recites a polypeptide which additionally comprises fragments of SEQ ID NOs: 16, 26 or 20. These fragments are not further identified or specified. As stated above, even if an active site, such as the extracellular domain (SEQ ID NO:22), is identified, the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore the presence of unspecified fragments of SEQ ID NOs:16, 26 or 20 may not be sufficient to retain the required activity or may interfere with the appropriate configuration of the extracellular domain such that the required activity may not be maintained. Furthermore, one would be unable to predict that the fusion polypeptide would function as an antagonist of expression and/or secretion of any unspecified cytokine.

In response to 2 and 3:

Applicants are directed to MPEP § 21645 which states:

> Applicant may submit **factual affidavits under** 37 CFR 1.132 or cite references to show what one skilled in the art knew at the time of filing the application. A declaration or affidavit is, itself, evidence that must be considered. The weight to give a declaration or affidavit will depend upon the amount of factual evidence the declaration or affidavit contains to support the conclusion of enablement. *In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) ("expert's opinion on the ultimate legal conclusion must be supported by something more than a conclusory statement"); *cf. In re Alton, 76* F.3d 1168, 1174, 37 USPQ2d 1578, 1583 (Fed. Cir. 1996) (declarations relating to the written description requirement should have been considered).
>
> Applicant should be encouraged to provide any evidence to demonstrate that the disclosure enables the claimed invention.
> **To overcome a *prima facie* case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing.**

Exhibit A, submitted by Applicants, has not been submitted as a declaration or affidavit, nor is the data contained within submitted as a publication from a referenced journal. It is therefore difficult for the Examiner to evaluate the submitted data.

Therefore, the data submitted cannot be considered to impact on the patentability of the instant invention.

Applicants have also submitted post-filing date art, Chung et al and Moh et al. Chung et al. teach that *hepaCAM* gene encodes an Ig-like transmembrane glycoprotein which may be involved in cell-matrix interaction and cell growth regulation (page 840, 2nd column, last paragraph). Moh et al teach that hepaCAM modulates cell-matrix interaction (page 27374, 2nd column, last paragraph) and mediates increased cell motility (page 27374, 1st column, 2nd paragraph. In an *in vitro* wound healing assay, cells transfected with hepaCAM filled more of the scratched area than cells transfected with vector alone. It is noted that Applicants have not taught stimulation of wound healing as a claimed utility for the polypeptide of the instant invention. Neither of the submitted publications teach that the hepaCAM polypeptide functions as an antagonist of cytokine expression and/or secretion or provides teaching to support the full scope of the claims, that is that the polypeptide of the instant invention can be used for therapy or diagnosis of any unspecified inflammatory disease, autoimmune disease liver disease or liver failure.

In response to 4: Applicants argue that the specification teaches the skilled person to identify fragments that contain an immunoglobulin domain (page 8 of the application as filed) and the functional importance of this domain (page 16, line 4-9 of the application as filed). However, the claims do not recite that the "fragment of a polypeptide" must comprise the extracellular immunoglobulin domain. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, as stated above, one would be unable to predict that said polypeptide would function as an antagonist of expression and/or secretion of **any, unidentified cytokine.**

Therefore, the rejection is maintained.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The rejection of Claims 1, 10-15, 20, 21 and 78 under 35 U.S.C. 102 (e) as being anticipated by Baughn, *et al* (WO0240671, publication date 23 May 2002, priority claimed to provisional application 60/249,645, 16 November 2000, cited in previous Office Action) is maintained for reasons of record and for reasons set forth below.

Claim 1 is drawn to a fusion protein comprising a fragment of a polypeptide according to i) or ii) fused to a heterologous polypeptide wherein the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO:22. Thus, the limitations of the claim are anticipated by art which teaches a fusion polypeptide comprising a fragment of SEQ ID NOs:16, 26, or 20 wherein the polypeptide comprises an extracellular domain as recited in SEQ ID NO:22.

Baughn et al. teach a polypeptide, identified as IGSFP-4 which is 100% identical to amino acids 1-240 of SEQ ID NO:20 and comprises a polypeptide (amino acid residues 34-240) which is 100% identical to SEQ ID NO:22 domain of the mature INSP052 polypeptide. Additionally, Baughn et al. teach a polypeptide (AAE14784) comprising a sequence which is 100% identical to amino acids 1-291 of SEQ ID NO:16 of instant invention. Furthermore, this sequence comprises a sequence which is 100% identical to amino acids 1-258 of SEQ ID NO:26 of the claimed invention. Thus, Baughn et al teach a polypeptide which comprises fragments of SEQ ID NOs: 16, 26, or 20 and comprises the amino acid sequence of SEQ ID NO:22.

The reference teaches fusion proteins comprising an IGFSP protein ligated to a heterologous protein sequence, fusion proteins comprising an IGFSP protein and a short cationic N-terminal portion from the HIV Tat-1 protein), and fusion proteins

comprising IGFSP protein and glutathione S-transferase, or a peptide epitope tag. Thus, the reference teaches a fusion protein comprising a fragment of SEQ ID NOs:16, 26, or 20 wherein the polypeptide comprises an extracellular domain as recited in SEQ ID NO:22. The reference teaches that IGFSP plays a role in immune disorders and may be administered to treat a number of diseases, including auto-immune and inflammatory diseases, thereby teaching a polypeptide that functions as an antagonist of cytokine expression and/or secretion.

Applicants traverse the rejection (Response of 15 September 2008, page 19, 1st paragraph). The reasons for the traversal are:

Baughn et al. does not disclose the existence of an extracellular domain in the IGFSP-4 polypeptide let alone the sequence of this domain. It does not therefore disclose an isolated polypeptide comprises or consists of i), ii), or iii), and that the polypeptide additionally comprises an extracellular domain as recited in SEQ ID NO: 22, and that the polypeptide functions as an antagonist of cytokine expression and/or secretion, and therefore fails to teach or suggest all of the elements of the pending claims. That is, Baughn *et al.* fails to teach an isolated polypeptide that comprises one of SEQ ID NOs: 16, 20 or 26 in combination with SEQ ID NO:22, wherein the polypeptide functions as an antagonist of cytokine expression and/or secretion.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Baughn et al. teach a polypeptide, identified as IGSFP-4 which is 100% identical to amino acids 1-240 of SEQ ID NO:20 and comprises a polypeptide (amino acid residues 34-240) which is 100% identical to SEQ ID NO:22. While Baughn et al does not specifically identify this fragment as the extracellular domain, absent evidence to the contrary, proteins that comprise sequences that are 100% identical to the sequences of SEQ ID NOs:20 and 22 would have the same function as the extracellular domain of the polypeptide of the instant invention.

While the teachings of Baughn et al do not specifically identify IGFSP-4 as a cytokine antagonist, case law has established that the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the

prior art's functioning, does not render the old composition patentably new to the discoverer. *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Also, case law has established that a compound and all of its properties are inseparable, as are its processes and yields (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Absent evidence to the contrary, a protein that comprises an amino acid sequence of 100% homology to that of SEQ ID NO:20 or 22 would have the same functional activity; namely, it would function as a cytokine antagonist. Applicant's assertion that the polypeptide of the instant invention functions as a cytokine antagonist was already inherent in the Baughn reference. If the Baughn reference would have attempted to measure the effect of IGFSP-4 on cytokine activity, they would have uncovered it. Thus, the Baughn document anticipates the claimed invention of the instant application.

Furthermore, inherent anticipation does not require that one of ordinary skill in the art recognize an inherent feature in a prior art disclosure (*Schering Corp. v. Geneva Pharmaceuticals Inc.*, 67 USPQ2d 1664 (CAFC 2003); *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)).

Applicants are reminded that the invention of Claim 1 is claimed using Markush language. The claim is drawn to an isolated polypeptide which polypeptide may be i) or ii) or iii). Baugn et al teaches a fusion protein comprising a fragment of SEQ ID NOs:16, 26, or 20 wherein the polypeptide comprises an extracellular domain as recited in SEQ ID NO:22, thus teaching the limitations of part iii of claim 1. The Office has met its burden by citing art that anticipates the limitations of any one of the portions of claim 1; the art does not have to anticipate all of the portions (i-iii) of claim 1.

Thus the rejection is maintained.

Conclusion:

No claims are allowed.

In light of new grounds of rejection, this Office Action is made non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. H. S./
Examiner, Art Unit 1647

/Manjunath N. Rao, /
Supervisory Patent Examiner, Art Unit 1647